INTERNATIONAL CONFERENCE ON HARMONISATION OF TECHNICAL REQUIREMENTS FOR REGISTRATION OF PHARMACEUTICALS FOR HUMAN USE

DRAFT CONSENSUS GUIDELINE

STABILITY DATA PACKAGE FOR REGISTRATION IN CLIMATIC ZONES III AND IV

Released for Consultation
at *Step 2* of the ICH Process
on 7 February 2002
by the ICH Steering Committee

At Step 2 of the ICH Process, a consensus draft text or guideline, agreed by the appropriate ICH Expert Working Group, is transmitted by the ICH Steering Committee to the regulatory authorities of the three ICH regions (the European Union, Japan and the USA) for internal and external consultation, according to national or regional procedures.

This draft guidance, when finalized, will represent the Food and Drug Administration's (FDA's) current thinking on this topic. It does not create or confer any rights for or on any person and does not operate to bind FDA or the public. An alternative approach may be used if such approach satisfies the requirements of the applicable statutes and regulations.

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1. INTRODUCTION

1.1 Objectives of the Guideline

This guideline defines an approach for broader utility of the ICH Q1A(R) guideline on Stability Testing of New Drug Substances and Products (hereafter referred to as the parent guideline) for territories in Climatic Zones III and IV. (See Schumacher P., Aktuelle Fragen zur Haltbarkeit von Arzneimitteln [Current questions on drug stability] *Pharmazeutische Zeitung*, 1974, 119:321-324)

1.2 Background

The parent guideline defines the stability data package for the ICH tripartite regions (EC, Japan, and the United States). For other territories in Climatic Zones I or II, the parent guideline could be considered applicable, because the long term and accelerated storage condition defined within the guideline are based on an evaluation of climatic data from Zone II (which can be considered to cover Zone I, since Zone II is less temperate).

For territories in Climatic Zones III and IV, the data package as described in the parent guideline can be considered applicable except for the defined long term storage condition.

The World Health Organisation (WHO) has published a guideline on "Stability testing of pharmaceutical products containing well established drug substances in conventional dosage forms" (WHO Technical Report Series, No 863, Annex 5), updated in the Report of the thirty-seventh meeting of the WHO Expert Committee on Specifications for Pharmaceutical Preparations, Geneva, 22-26 October 2001. It defines stability testing recommendations, including storage conditions for all four climatic zones. To facilitate the presentation of a global stability data package, thereby enabling timely access to new medicines in all territories of the world, harmonised global stability testing recommendations have been established based on the parent guideline and the WHO guideline.

1.3 Scope of the Guideline

This document is an annex to the parent guideline and recommends the long term storage condition to determine the data package considered sufficient for a registration application for drug substances and products intended to be marketed in Climatic Zones III and IV.

2. GUIDELINES

2.1 Continuity with the Parent Guideline

This guideline should be read in conjunction with the parent guideline and subsequently published annexes (Q1B, Q1D, Q1E). The recommendations in the parent guideline and annexes should be followed unless specific alternatives are described within this annex.

The following sections of the parent guideline can be considered common to any territory in the world and are not reproduced here:

- Stress testing
- Selection of batches
- Container closure systems
- Specifications
- Testing frequency
- Statements/labelling
- Refrigerated storage
- Freezer storage
- Semi-permeable or impermeable containers

2.2 Storage Conditions

For Climatic Zones III and IV, the recommended long term and accelerated storage conditions for the "General case" (as described in the parent guideline) are shown below:

Study	Storage condition	Minimum time period covered by data at submission
Long term	30°C ± 2°C/65% RH ± 5% RH	12 months
Accelerated	40°C ± 2°C/75% RH ± 5% RH	6 months

For drug substances and products intended for registration applications within the ICH Tripartite regions, the parent guideline applies and long term testing will typically be conducted at 25°C ± 2°C/60% RH ± 5% RH. Where significant change occurs at any time during 6 months' storage at the accelerated condition, additional testing at the intermediate storage condition (30°C ± 2°C/65% RH ± 5% RH) should be conducted. Long term testing at 30°C ± 2°C/65% RH ± 5% RH can be a suitable alternative to 25°C ± 2°C/60% RH ± 5%. In this case, for an application in the ICH Tripartite regions, no testing at 25°C ± 2°C/60% RH ± 5% RH need be performed.

[Note: to harmonise the intermediate storage condition for Zones I and II with the long-term condition for Zones III and IV, the intermediate condition for the general case in the parent guideline will be changed to 30°C ± 2°C/65% RH ± 5% RH when this guideline reaches step 4]

Where appropriate, photostability testing should be conducted in accordance with the guidance given in ICH Q1B.

2.3 Cautionary Note on Data Packages for Climatic Zones III and IV

It should be noted that not all drug substances and products intended for markets in Zones I and II in particular container closure systems will be suitable for Zones III and IV. In this case, a reduced retest period or shelf life should be considered. Alternatively, a more protective container closure system could be called for.

However, there may be examples in which a product cannot be demonstrated to be stable when stored at 30°C ± 2°C/65% RH ± 5% RH. In this case, additional cautionary statements in the labeling can be appropriate.

If special transportation and storage conditions are identified as being outside the proposed storage criteria, additional study data should be made available, for example up to 3 months at 45–50°C and for Zone IV, 75% relative humidity (RH).